UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/105,117	06/17/1998	MARINA VRLIJC	FJ-122	5178

7590 12/03/2003

KLAUS J BACH
4407 TWIN OAKS LANE
MURRYSVILLE, PA 15668

EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Advisory Action	Applicati n No.	Applicant(s)	
	09/105,117	VRLIJC ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

--The MAILING DATE of this communication appears on the cover sheet with the corresp ndenc address --

THE REPLY FILED 18 August 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): Claims 43, 46-48 under 35 U.S.C. 101.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *43 and 46-48*.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-8 and 10-20*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 5

The amendment and response filed August 18, 2003 is acknowledged. Claims 1, 8, 16, 18, 19, 43, 46-48 have been amended. Claims 9, 21-42, 44, 45 are canceled. Therefore, Claims 1-8, 10-20, 43, 46-48 are currently pending.

The **objection to claims** 1, 8, 16, 18 and 19 is withdrawn in view of Applicants' amendments to claims.

Claims 43, 46-48 rejected under **35 U.S.C. 101** is withdrawn in view of Applicants' amendment to claims.

Claims 1-8 and 10-20 rejected under **35 U.S.C. 112, second paragraph**, is withdrawn in view of Applicants' response/remarks at page 8 (paper #49).

Claims 1 and dependent claims 2-8 and 10-20 stand/are rejected under **35 U.S.C. 112, first paragraph**, for the reasons set forth in the prior office action.

Pages 7 and 8 of applicants' response (filed August 18, 2003) argue (page 7, second paragraph) that the rejection is unreasonable. The comment is unpersuasive for reasons of record in the prior office action.

The third full paragraph of page 7 (paper #49) refers to specification page 6, lines 20-29 and J. Bacteriology, 1995, 177, 4021-4027 as support for classical mutagenesis. The expected results are asserted to be in SEQ ID NO: 2, however, these lines of the specification and SEQ ID NO: 2 along with the Vrljic et al. (Bacteriology, 1995, 177, 4021-4027) reference do not appear to demonstrate specificity to mutagenesis. Note that the process set forth in Vrljic et al. reference is random mutagenesis using N-methyl-N-nitro-N-nitrosoguanidine. Thus applicants comments are unpersuasive as to obtaining exactly what is set forth in SEQ ID NO: 2.

In the last full paragraph of page 7, it is noted that applicant refers to a process of screening, stating that the increased export can be determined in analogy according to example (second half of page 13-14, line 4), that is by silicon oil centrifugation and high pressure liquid chromatography (J. Chromat., 1983, 266, 471-482). In response it should be noted that second half of page 13 (and example e) and f)) describes a generic method,

however no description or Examples are provided for the enablement of claimed variants. Please see previous office action and discussion given below.

Claim 1 and the dependent claims 2-8 and 10-20 thereto are directed to a process for the microbial production of amino acids using a gene construct, having an export gene that encodes an amino acid sequence of SEQ ID NO: 2, wherein the regulatory gene of the construct encodes an amino acid sequence as set forth in SEQ ID NO: 3. Claim 1 also encompasses an increased production of amino acids in accordance with export gene expression endogenous to said microbial organism by selecting a step of mutating the export carrier gene such that an export carrier with increased export activity is generated.

Applicants assert at page 7 that the Examiner's objections for example that no enablement is provided for the feature "mutating the export carrier gene such that an export carrier with increased export activity is generated" is contradicted. Further, an explanation states, "firstly the steps given would be absolutely clear to a person." Next Applicants indicate that it has been stated at page 5, lines 17-20 (it should be lines 1-4, typo error) of the specification it is said that "an increase of the enzyme activity can be obtained for example by an increased substrate consumption achieved by changing the catalytic center or by eliminating the effects of enzyme inhibitors. In response, it should be noted that the objection is not to the concept or the feature (mentioned supra). The objection is to the absence of adequate guidance in the specification. It was stated in the previous office action that the specification, however, only discloses cursory conclusions (see page 6), without data to support the findings, which state that in general a functional derivative that can be obtained by deletion, insertion and/or substitution, wherein the regulator protein activity or function is retained or even increased, however the specification fails to provide a specific description or a demonstration of any mutant of export carrier gene and/or regulator gene that retains the activity of wild type. There are no indicia that the present application enables the full scope in view of the amino acid sequences corresponding to an export gene and a regulatory gene products as set forth in SEQ ID NO: 2 and SEQ ID NO: 3 or a mutant thereof as discussed in the stated rejection of the previous office action. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is encompassed.

Further Applicants urge that since a concrete possible way of how to obtain export carrier mutants is given, there is certainly not the burden of undue experimentation. This argument was addressed in the final rejection (paper # 48). The specification at page 6 provides a generic description for obtaining variants by deletion, insertion and/or substitution of nucleotides of corresponding sequences, wherein however the regulator protein activity or function is retained or even increased. Furthermore, the specification describes and demonstrates the production and increased accumulation of L-lysine by export gene (LysE) and regulator gene (LysG) in Examples e) and f) at page 13-14, however no description or Examples are provided for the enablement of claimed variants. The experimentation involved to enable the invention may constitute routine experimentation, however, because of the limited information in the specification it would require undue and excessive experimentation. No specific description is provided about the position of the corresponding sequence of SEQ ID NO: 2 and SEQ ID NO: 3 where amino acid substitution is suggested neither any activity of those variants have been demonstrated. Without more guidance from the specification it would require an undue and excessive experimentation for a person having skill in the art to be able to make and use the claimed analogs.

Rita Mitra, Ph.D.
November 19, 2003

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600